CME review article

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The approach to pediatric cough

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Objective: To provide an overview of pediatric cough, with specific emphasis on various causes, to aid in diagnosis and treatment.

Data Sources: Relevant articles and references published between January 1, 1961, and May 1, 2009, were found through a PubMed search using the following keywords: *pediatric cough* and *cough in children*.

Study Selection: All key relevant articles and textbook sections were reviewed, and the most relevant were selected for inclusion in this review.

Results: Although asthma, gastroesophageal reflux disease, and postnasal drip can be causes of cough in children, it is important to think of other potential causes, such as bronchitis, postviral cough, and foreign-body inhalation. Testing and treatment for cough will vary, depending on the presentation and diagnosis. Just as in adults, in children, the cause of cough can be multifactorial.

Conclusions: Pediatric cough is commonly encountered by primary care physicians and allergists. Physicians should be aware of the various potential causes of cough in children to properly determine the cause so that testing and treatment can proceed appropriately.

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INTRODUCTION

Cough is a common cause of health care visits among children. Although 1 report[1] suggested that healthy children may cough as many as 34 times in a 24-hour period, cough still can be distressing not only for children (causing such problems as interference with sleep) but also for caregivers and educational staff. Pediatric cough is classified into acute (lasting <2 weeks), subacute (lasting 2–4 weeks), and chronic (lasting >4 weeks). Patients with acute cough may develop subacute and chronic cough if the cause of the cough is not defined and adequately treated.

Although asthma, postnasal drip, and gastroesophageal reflux disease (GERD) are common causes of chronic cough in adults, these may not be as common in children. Pediatric cough is commonly encountered not only by primary care physicians but also by allergists; thus, it is important to be knowledgeable about their causes and management. Cough in children should be treated based on etiology, and there is no evidence for using medications for the symptomatic relief of cough in children.[2] Occasionally, short-term therapeutic trials with specific medications targeting a specific disease are justified. In addition, billions of dollars are wasted on marginally effective medications that may provide no greater benefit compared with placebo in suppressing cough, especially in children.[3] The purpose of this article is to review the differential diagnosis and approach to pediatric cough. Relevant articles and references published between January 1, 1961, and May 1, 2009, were found through a PubMed search using the following keywords: *pediatric cough* and *cough in chil-*

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UPPER AIRWAY COUGH SYNDROME

Upper airway cough syndrome is usually due to postnasal drainage, which causes irritation or inflammation of upper airway receptors. In children with the common cold, upper airway cough syndrome is the most common cause of acute cough.[4] Sinusitis and allergic rhinitis can be causes of postnasal drip that aggravates cough, and other causes of intermittent postnasal drainage in children include crying and other emotions, as well as irritants, temperature, and humidity changes.[5]

ARNOLD NERVE

Stimulation of the auricular branch of the vagus nerve (typically by a foreign body in the ear canal) can trigger cough. Also, stimulation of the posterior-inferior wall of the external acoustic meatus can elicit coughing.[6] There have been reports of chronic cough associated with ear canal stimulation from wax impaction.[7]

INFECTIONS

The most common cause of cough in children is acute viral upper respiratory tract infection.[8] The frequency of upper respiratory tract infections and associated cough is heightened when children first attend a daycare facility and averages approximately every 3 weeks in this initial period.[9] Cough due to upper respiratory tract infection typically resolves by 3 weeks.[9] Infectious causes of cough in children include viruses, as well as pertussis, mycoplasma, *Chlamydia pneumoniae*, fungi, and parasites.[5]

Lower respiratory tract infections include acute bronchitis and pneumonia. Acute bronchitis is an acute respiratory infection characterized by cough, with or without phlegm, that lasts up to 3 weeks and is usually self-limiting.[10] Respiratory viruses, such as influenza, parainfluenza, and respiratory syncytial virus, are the most common causes of acute bronchitis, whereas bacteria cause less than 10% of infections.[5] Among bacterial causes of acute bronchitis, *Mycoplasma pneumoniae*, *C pneumoniae*, *Bordetella pertussis*, and *Bordetella parapertussis* are the most common causes.[11] The pathogenesis of acute bronchitis involves mucosal injury, epithelial cell damage, and the release of proinflammatory mediators.[12] Typical features of pneumonia include fever, cough, dyspnea, abnormal chest examination results (rales or decreased breath sounds), and abnormal chest radiograph (in which patchy infiltrates, atelectasis, hilar adenopathy, or pleural effusion may be observed).[13] *Streptococcus pneumoniae* is the most prevalent bacterial pathogen, but the spectrum of potential pathogens to be considered includes *Chlamydia trachomatis*, *C pneumoniae*, *Chlamydia psittaci*, *Coxiella burnetii*, *Pneumocystis jiroveci*, *B pertussis*, *M pneumoniae*, *Legionella pneumophila*, and respiratory viruses.[13]

Pertussis can also be a cause of cough in children; there has been a recent resurgence in cough due to pertussis, and the number of pertussis infections has quadrupled in North America during the past 10 years. A catarrhal phase occurs in the first week, followed by a cough that becomes paroxysmal and intense, with occasional expulsion of a thick plug consisting of inspissated tracheal secretions and necrotic epithelium.[5] The cough lasts at least 2 weeks and can be accompanied by posttussive emesis. Then there is a convalescent phase of gradual decrease in cough frequency and intensity, lasting 6 to 12 weeks; after 3 weeks of cough, the likelihood of culturing *B pertussis* is minimal, and polymerase chain reaction gives a higher yield.[14]

POSTINFECTIOUS COUGH

Postinfectious cough may last for more than 3 weeks but less than 8 weeks, and many cases of subacute cough are due to postinfectious cough. Epithelial disruption and inflammation by neutrophils and lymphocytes are thought to play a central role in postinfectious cough; airway inflammation promotes mucous production, which promotes cough to expel retained secretions.[15] It has been reported that postnasal drainage during upper respiratory tract infections can cause reversible upper airway obstruction with cough.[16]

ASTHMA

Asthma is an inflammatory disease of the airways characterized by reversible airway obstruction, cough, wheezing, shortness of breath, or chest tightness. Some patients may have cough variant asthma in which cough is the sole manifestation of asthma.[17] Patients with cough variant asthma demonstrate airway hyperresponsiveness to methacholine challenge, can show an obstructive pattern on spirometry, and respond to bronchodilators and corticosteroids. A heightened cough reflex sensitivity appears to be a feature of both cough variant asthma and other cases of asthma in which cough is a major symptom; in some cases, cough variant asthma may be a precursor of classic asthma.[18] A complete discussion of asthma is beyond the scope of this article; however, it is important to think of asthma in the differential diagnosis of pediatric cough, especially chronic cough.

INHALATION OF FOREIGN BODY

Cough of sudden onset in a child should alert the physician to the possibility of foreign-body inhalation. Cough is the most common symptom in some series of foreign material inhalation but not in others,[19] and a history of a choking episode is absent in approximately 50%.[20] In addition, chest x-ray examinations produce normal results in approximately 20% to 40% of children who are found to have a foreign body on bronchoscopy.[9] A previously missed foreign-body inhalation can present as chronic cough, and missed foreign bodies in the airway can lead to permanent lung damage.[21] Rarely, tonsilloliths (tonsil stones or calculi composed of hardened material that contain a combination of food particles, bacteria, oral debris, and white blood cells in a concentrically

laminated pattern) form in the tonsillar crypts and can be a source of foreign-body aspiration, and recurrent episodes can be a cause of chronic cough.[5]

HABIT COUGH

Habit cough, which has been denoted by various terms, such as *psychogenic cough* and *cough tic*, is characterized by a loud honking or barking cough, disruption of normal activities, and frequent presence of secondary gain (such as school absence). It is frequently preceded by upper respiratory tract infection and often is worsened in the presence of parents, teachers, and health care professionals. Habit cough is a diagnosis of exclusion and usually responds to behavioral modification techniques rather than pharmacotherapy. A more detailed review of habit cough is available in a previous issue of the *Annals*.[22]

ATOPIC COUGH

Atopic cough is characterized by chronic cough without other respiratory symptoms, normal airway responsiveness to methacholine, and an excess of eosinophils in induced sputum and bronchial biopsy specimens.[18] It presents as a nonproductive cough in patients with allergies, and the cough is resistant to treatment with bronchodilators. Unlike patients with cough variant asthma, atopic cough patients do not progress to wheezing if they fail to be treated with inhaled corticosteroids.[23]

VOCAL CORD DYSFUNCTION

Vocal cord dysfunction (VCD) can often complicate cough. VCD is characterized by paradoxical adduction of the vocal cords, with resultant airflow limitation at the level of the larynx; adduction usually occurs during inspiration, but it can also occur during expiration.[24] The degree of vocal cord adduction can vary, and not all patients display posterior chinking seen on rhinolaryngoscopy.[25] In many instances, transient VCD follows an upper respiratory tract infection with coughing paroxysms due to postnasal drainage inducing VCD.[26]

BRONCHIOLITIS

Bronchiolitis typically affects the smaller airways ($<$2 mm in diameter) that do not have cartilage in their walls.[27] Various factors contribute to cough in bronchiolitis, including airway inflammation, fibrosis, architectural distortion of the small airways with and without mucous hypersecretion, and bronchial hyperresponsiveness.[5] Bronchiolitis has various causes, including infections (such as from respiratory syncytial virus), inhalation of smoke or sulfur dioxide, collagen vascular disease, inflammatory bowel disease, immunodeficiencies, and drug reactions (such as nitrofurantoin).[28] Chest radiographs may produce normal results, but clues that suggest bronchiolitis include dilation or airway wall thickening appearing as 2- to 4-mm nodular branching and linear branching with "tree-in-bud" appearance on high-resolution computed tomography.[5]

TUBERCULOSIS

Cough may be the sole presentation in tuberculosis, and patients may not present with typical symptoms (such as night sweats, hemoptysis, weight loss, and fatigue). Suggestive radiographic findings include upper lobe infiltrates, cavitary infiltrates, and hilar or paratracheal adenopathy.[29] A tuberculin skin test result (Mantoux) with induration of greater than or equal to 10 mm at 48 to 72 hours is generally considered positive in patients at medium risk of infection; such risk factors include current or previous residence in high-prevalence areas (Asia, Africa, Latin America), homelessness or residence in correctional institutions, intravenous drug use, recent weight loss or malnutrition, leukemia, Hodgkin disease, diabetes mellitus, and age younger than 4 years.[30] Induration of greater than or equal to 5 mm is considered a positive result in patients at high risk of infection; such risk factors include recent close contact with a case of active tuberculosis, chest x-ray film compatible with tuberculosis, human immunodeficiency virus infection, and immunocompromise (chemotherapy, organ transplantation, and systemic glucocorticoid treatment [equivalent to $\geq$15 mg/d of prednisone for $\geq$1 month]).[30,31] For children 4 years and older without the aforementioned risk factors, induration size of 15 mm or greater is considered a positive test result.[30] The tuberculin skin test is not 100% sensitive; even among patients with proven tuberculosis and apparent immunosuppression, 10% to 20% have negative skin test results.[32]

BRONCHIECTASIS

Bronchiectasis in children may be associated with cystic fibrosis, allergic bronchopulmonary aspergillosis, middle lobe syndrome, immotile cilia syndrome, and pneumonia.[5] Bronchiectasis may be seen in asthma, but asthma itself does not cause bronchiectasis. In those with asthma and bronchiectasis, spirometry does not necessarily correlate with the severity of the symptoms.[33] Middle lobe syndrome is a condition mostly seen in young children with atelectasis or recurrent pneumonitis of the right middle lobe or lingula.[5] Cough due to bronchiectasis can occur in immunodeficiency syndromes, such as common variable immunodeficiency and specific antibody deficiency. High-resolution computed tomography of the chest revealing peripheral airway lumen diameters larger than adjacent artery diameters and with retained secretions can be helpful in defining bronchiectasis in patients with subtle findings of airway streaking or air bronchograms on chest radiography.[34]

GERD AND LARYNGOPHARYNGEAL REFLUX

Gastroesophageal reflux is a physiologic event that occurs upward of 50 times a day in healthy individuals without producing symptoms; it becomes GERD when accompanied by symptoms and/or mucosal damage.[5] One mechanism by which GERD is believed to cause cough is the esophageal vagal reflex theory; irritation of the esophagus sends signals to vagal afferent nerves, then to the nucleus tractus solitarius

Table 1. Procedures for Diagnosing Gastroesophageal Reflux Disease and Laryngopharyngeal Reflux[5]

Procedures	Comments
Barium swallow	Poor sensitivity
Technetium scintiscan	Poor sensitivity
Esophagogastroduodenoscopy	Does not identify reflux as a cause of cough
Rhinolaryngoscopy	Identifies inflammation due to laryngopharyngeal reflux
Single channel pH probe	Misses proximal esophageal reflux
Dual channel pH probe	Considered the "gold standard" but misses bolus
pH telemetry (Bravo capsule)	Requires esophagogastroduodenoscopy for placement
Esophageal manometry	Detects bolus movement independent of pH
Multichannel intraluminal impedance[a]	Detection of secretions independent of pH

[a] Combining multichannel intraluminal impedance with pH monitoring provides the best opportunity to define bolus and microaspiration whether or not bolus is acidic.

in the medulla oblongata. The nucleus ambiguous is close to the tractus solitarius and serves to innervate motor reflexes via parasympathetic response, promoting bronchoconstriction.[35] The motor nucleus retroambiguus then signals to the muscles of the chest wall, triggering cough. Another mechanism by which GERD is thought to trigger cough is microaspiration of gastric contents. Reflex cough from distal esophageal acidification and stimulation of cough receptors and nonacid volume reflux are also proposed mechanisms by which gastroesophageal reflux causes cough.[9]

Laryngopharyngeal reflux (LPR) can be a cause of cough and is usually visualized by rhinolaryngoscopy. Patients with LPR have various changes seen on rhinolaryngoscopy, including vocal cord edema, subglottic edema, and/or swelling of the posterior commissure.[36] Bronchoscopy may reveal signs of aspiration, such as subglottic stenosis, hemorrhagic tracheobronchitis, and erythema of subsegmental bronchi.[37]

Esophagogastroduodenoscopy may define GERD, but it does not identify GERD as the source of the coughing, and a normal esophagogastroduodenoscopy result does not rule out GERD as the cause of cough. Barium swallow is limited by poor sensitivity. A pH probe is considered to be the best procedure for defining GERD, with a positive predictive value of 89% and a negative predictive value of slightly less than 100%.[38] Table 1 summarizes the diagnostic tests available for evaluating GERD and LPR causing reflux.

OTHER CAUSES OF COUGH IN CHILDHOOD

Tourette syndrome may present with cough in children between the ages of 2 and 15 years and is not necessarily associated with outbursts of coprolalia. Phonic tics may mimic upper airway cough syndrome with clearing of throat, coughing, and grunting.[5]

Four percent of newborns have abnormalities in swallowing, and this may lead to neonatal aspiration syndrome.[5] Presence of gastric material in the lungs is found in 20% to 30% of sudden infant death syndrome autopsy results; furthermore, in animal models, aspiration of liquid into the airway has been shown to prevent autoresuscitation (which involves agonal breathing, thought to be an efficient survival mechanism seen in infants and young children with acute hypoxemia).[39] Congenital esophageal atresia and/or tracheoesophageal fistula can produce tracheomalacia, esophageal stricture, and gastroesophageal reflux.[5] A brassy, honking quality of the cough associated with dysphagia and recurrent pneumonia suggests aspiration as a cause and requires prompt evaluation for these types of abnormalities.[40]

Vascular rings, tracheomalacia, and Mounier-Kuhn syndrome (tracheobronchomegaly) can also be causes of cough in children. More than 75% of children with congenital tracheomalacia secondary to a congenital vascular anomaly have chronic cough.[41] Cough due to congenital airway malformations typically present with symptoms in early childhood; however, these malformations can be misdiagnosed or remain undiagnosed for many years.[9] Table 2 summarizes usual and unusual causes of cough in children.

TESTING AND TREATMENT OF PEDIATRIC COUGH

Testing and treatment for cough will vary, depending on the presentation and diagnosis. Tables 3 and 4 outline diagnostic tools and therapies for cough, respectively. Just as in adults, in children, the cause of cough can be multifactorial.

For patients with chronic cough, if there is a history of wheeze as a symptom along with other risk factors for asthma

Table 2. Causes of Cough in Children[5]

Usual causes	Unusual causes
Upper airway cough syndrome	Habit
Asthma	Neonatal aspiration
Vocal cord dysfunction	Vascular rings
Pneumonia	Croup
Bronchiectasis	Cystic fibrosis
Pertussis	Tourette syndrome
Gastroesophageal reflux	Tracheoesophageal fistula
Sinusitis	Tracheomalacia
Atopic cough	Mounier-Kuhn syndrome
Bronchitis	Foreign body in ear canal
Bronchiolitis	
Tuberculosis	
Aspiration of foreign body	

Table 3. Tests Available to Assist in Diagnosing Causes of Cough[5]

Test	Diagnosis
Spirometry	Asthma, cystic fibrosis
Skin testing or specific IgE	Allergic rhinitis, asthma
Methacholine challenge	Asthma
Sweat chloride, ΔF508 analysis	Cystic fibrosis
PCR analysis	Pertussis
High-resolution CT scan	Bronchiectasis
CT sinuses	Occult sinusitis
Multichannel intraluminal impedance	GERD or LPR
Rhinolaryngoscopy	Vocal cord dysfunction or laryngeal tumors

Abbreviations: CT, computed tomography; GERD, gastroesophageal reflux disease; LPR, laryngopharyngeal reflux; PCR, polymerase chain reaction.

Table 4. Therapeutic Options for Cough Based on Diagnosis[5]

Diagnosis	Treatment options
Upper airway cough syndrome	H_1-antihistamines with anticholinergic adverse effects
	Intranasal corticosteroids
	Intranasal ipratropium
Sinusitis	Antibiotics with or without intranasal corticosteroids
Asthma, atopic cough	Inhaled corticosteroids
Pertussis	Macrolide antibiotics
GERD or LPR	Proton pump inhibitors
Vocal cord dysfunction	Speech therapy, correction of UACS or LPR

Abbreviations: GERD, gastroesophageal reflux disease; LPR, laryngopharyngeal reflux; UACS, upper airway cough syndrome.

(family history of asthma, personal history of atopic dermatitis, sensitization to aeroallergens), a trial of low-dose inhaled corticosteroids for 2 to 4 weeks is appropriate; if after this trial there has been no improvement in cough, use of the inhaled corticosteroids should be stopped.[9]

Although diphenhydramine has been reported to have central antitussive action,[42] it should be noted that upper airway cough syndrome due to viral infection is not a histamine-mediated event, and thus antihistamines are ineffective.[5] For patients with postnasal drainage refractory to antihistamines (and in allergic rhinitis, intranasal corticosteroids and possibly leukotriene modifiers), intranasal ipratropium bromide provides the drying effect required with minimal adverse effects[43] and can be used in children older than 5 years. For patients with chronic upper airway cough syndrome and a history suggestive of allergic rhinitis, skin testing should be performed, and consideration should be given to immunotherapy (if indicated). In patients who do not respond to antihistamines and/or intranasal steroids for postnasal drainage causing chronic upper airway cough syndrome, sinus imaging should be considered to define occult sinusitis.[38]

For acute bronchitis, antibiotic treatment is not required because the causative organism is rarely defined.[5] The use of mucokinetic agents, such as guaifenesin, has not been shown to be beneficial and is therefore not recommended. For patients with bronchiectasis, therapy specific for the cause is required. In patients with suspected pertussis infection, a macrolide antibiotic is indicated, followed by isolation for 5 days from the start of treatment. The suspicion of pertussis should be raised in patients with cough lasting for at least 2 weeks without another apparent cause and accompanied by paroxysms of coughing, posttussive emesis, and/or an inspiratory whooping sound.[38] Early treatment of pertussis within the first 1 or 2 weeks will decrease the intensity and duration of coughing paroxysms; however, beyond this period, patients with pertussis are unlikely to respond to an antibiotic.[38] For patients with GERD, especially those with LPR, there may be better suppression of cough with twice-daily dosing of proton pump inhibitor rather than once-daily dosing.[44]

CONCLUSION

Cough in children can be distressing to patients, caregivers, and educational personnel, and the approach requires a careful history and detailed physical examination to help guide further testing and treatment. Although upper airway cough syndrome, asthma, and GERD are common causes of cough in adults, in children a broader approach is necessary, and particular attention needs to be paid to postviral cough, sinusitis, and protracted bacterial bronchitis.[8] In many cases, prolonged therapy will be required for any improvement to be noticed. Allergists are experts in the management of upper and lower airway disorders and can play an important role in the diagnosis and management of pediatric cough.

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